



1

How the Program Works



- Web-based program, CME, CNE, and CPE credit available
- Two parts, with a post-test after each part (note: ★ in upper right-hand corner of slides indicate post-test content)
- Brief polling questions periodically in each part
- Certificate available upon completion of post-tests and evaluation
- Additional resources, tools, and supplemental educational activities available at www.scopeofpain.org

2

Faculty



Faculty members have no relevant financial relationships to disclose.

This activity does include discussion of the off-label use of certain formulations of buprenorphine to treat pain. These formulations are approved to treat opioid use disorder but not to treat pain. This presentation does include discussion of the off-label use of clonidine and tizanidine to treat opioid withdrawal symptoms. Clonidine and tizanidine are not FDA approved for this use.

Daniel P. Alford, MD, MPH (Course Director)

Professor of Medicine
Associate Dean, Center for Continuing Education
Boston University Chobanian & Avedisian School of Medicine
Boston Medical Center

Erica J. Bial, MD, MS

Interventional Pain Specialist, Private Practice
Faculty, Tufts University | Medford, MA

Content Development Committee

Daniel P. Alford, MD, MPH (Course Director), Boston University Chobanian & Avedisian School of Medicine | Boston Medical Center
Erica Bial, MD, MS, Faculty, Tufts University, Medford, MA
Patrick Kelly, PharmD, University of Rhode Island College of Pharmacy
Kristin Wason, NP, Boston University Chobanian & Avedisian School of Medicine | Boston Medical Center

Planning

Ilana Hardesty, MA, Assistant Director, CCE Operations, Boston University Chobanian & Avedisian School of Medicine

3

3

Partners and Supporters



National Partner

- Federation of State Medical Boards

Opioid REMS

- Content dictated by FDA
"Blueprint for Prescriber Education"
- FDA requires opioid analgesic manufacturers to fund CME-certified education by approved providers

Grant Support

This activity is supported by an independent educational grant from the Opioid Analgesic REMS Program Companies. See https://opioidanalgesicrems.com/Resources/Docs/List_of_RPC_Companies.pdf for listing of REMS Program Companies. This activity is intended to be fully compliant with the Opioid Analgesic REMS education requirements issued by the US FDA.

4

4

About the Program



Through the case
presented in this
program, you will
learn how to:

- Assess pain and function
- Educate patients about opioid risks and limitations of benefit
- Assess for prescription opioid misuse risk
- Develop patient-centered treatment goals
- Monitor patients prescribed opioids for benefits and harms
- Use a risk-benefit framework when initiating, maintaining, modifying, or tapering opioid analgesics
- Diagnose and manage patients with opioid use disorder with or without concurrent pain

5

5

Purpose of the Training



- Covers strategies for safer use of opioids for managing pain by reviewing **best practices** and sharing **clinical pearls**
- Counts towards the **2023 DEA education requirement** of the **Medication Access and Training Expansion (MATE) Act**
- Aligns with the **2022 CDC Clinical Practice Guideline for Prescribing Opioids for Pain**
- Does NOT cover palliative care or end of life pain management

Alford DP, et al. *Pain Med.* 2016
Dowell D et al. *MMWR* 2022
https://deaddiversion.usdoj.gov/pubs/docs/MATE_Training_Letter_Final.pdf

6

6



Introduction: Setting the Stage

7

7

Pain: “An Unpleasant Sensory and Emotional Experience”

Acute Pain

*Life sustaining
symptom*

Adaptive eliciting
motivation to
minimize harm
and allow healing

Chronic Pain

Pain persisting beyond expected healing (~3 months)
No evolutionary benefit, can be a disease in and of itself

Maladaptive disorder influenced by genetics and epigenetics;
categorization influences work-up, treatment, and prognosis

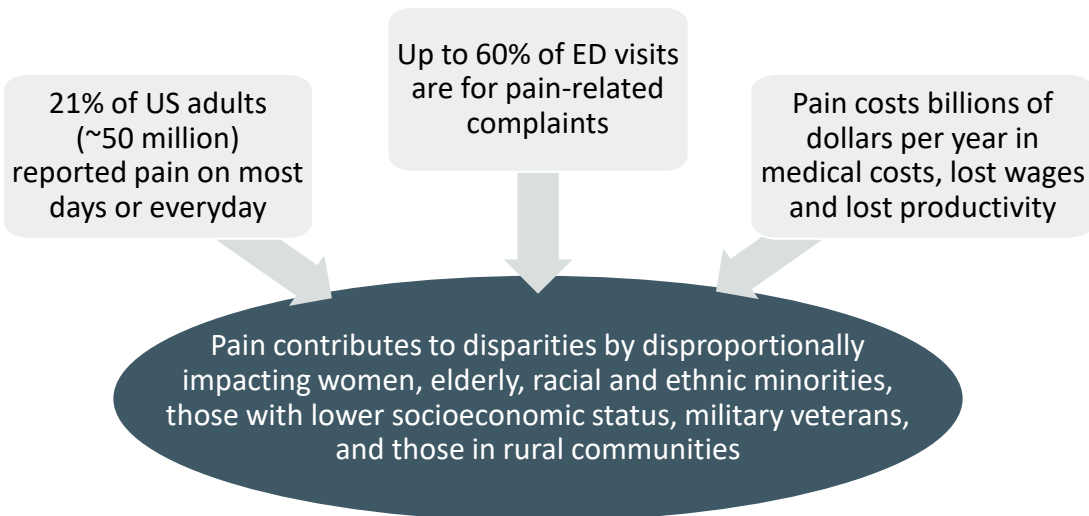
- **Nociceptive**: actual or threatened tissue damage – **somatic** (e.g., bones, joints, muscle) and **visceral** (e.g., mucosal injury, obstruction/distention, ischemia)
- **Neuropathic**: disease or injury of the somatosensory nervous system – **central** (e.g., traumatic, vascular, neurodegenerative) and **peripheral** (e.g., compression)
- **Nociplastic**: abnormal pain processing without evidence of tissue damage or discrete pathology – **diffuse sensitization** (fibromyalgia), **regional sensitization** (complex regional pain syndrome), **visceral pain** (irritable bowel syndrome),
- **Mixed Pain**: combination of the different types of pain, occurring simultaneously in the same area of the body

Raja SN, et al. *Pain*. 2020
Cohen SP, et al. *Lancet*. 2021
Fitzcharles MA et al. *Lancet*. 2021
Clauw DJ et al. *Postgrad Med*.
2019
Freynhagen R et al. *Curr Med Res
Opin*. 2020

8

8

The State of Pain



Yong R et al. *Pain* 2022
Cordell WH, et al. *Am J Emerg Med.* 2002

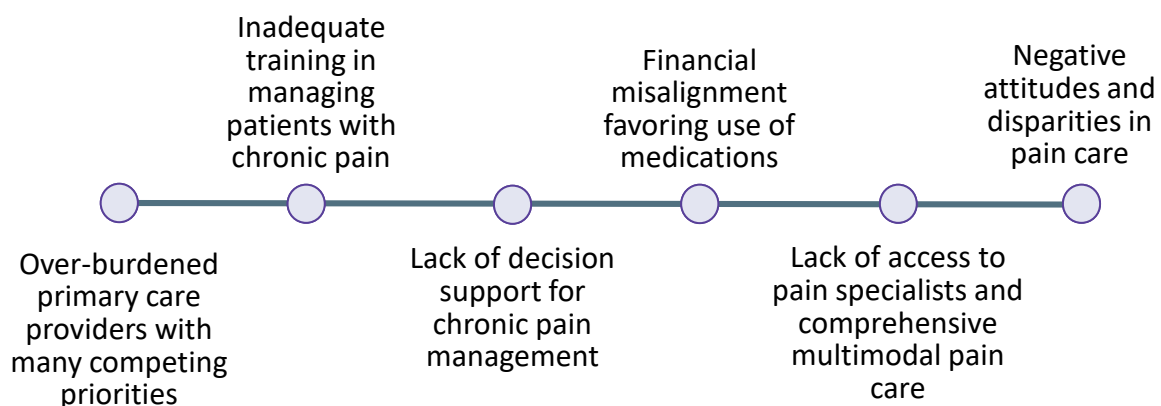
Gaskin DJ, Richard P. *J Pain* 2012

Dahlammer J et al. *MMWR* 2018
Mills SEE et al. *Br J Anaesh.* 2019

9

9

Barriers to Adequate Pain Care



10

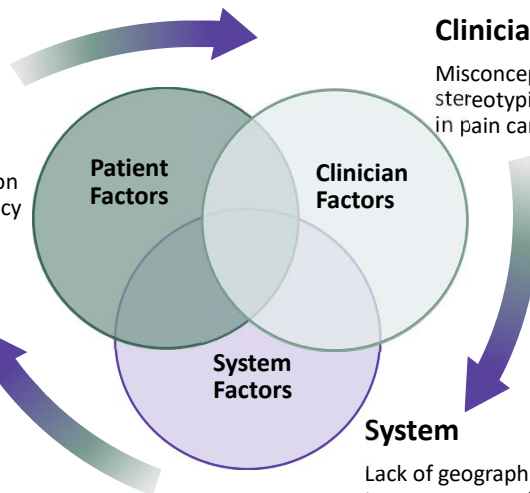
10

Disparities in Pain Care

*Racial minorities and vulnerable populations experience additional pain and suffering because of disparities in access and treatment**

Patient

Language barriers, cultural differences in communication and beliefs and health literacy can lead to poor pain treatment outcomes



Clinician

Misconceptions, negative attitudes, stereotyping, implicit bias result in disparities in pain care

System

Lack of geographic and/or financial access to care, poor socioeconomic status

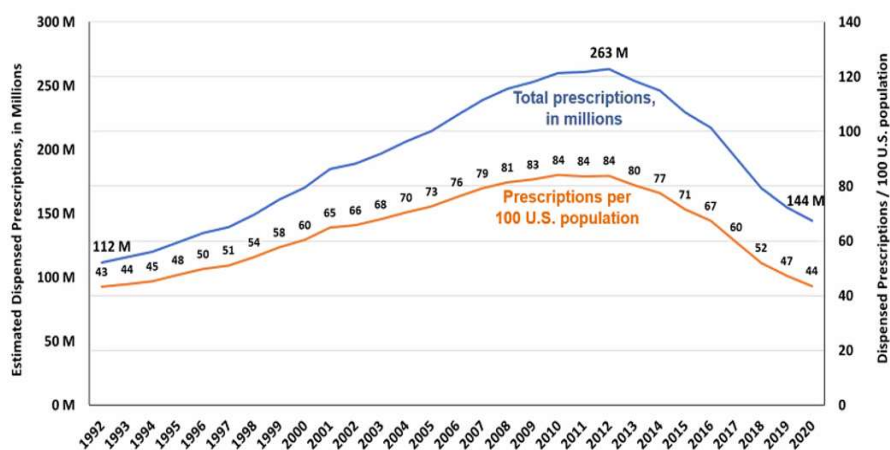
Meints SM, et al. *Pain Manage.* 2019

*Nguyen LH, et al. *Anesthesiology Clinics.* 2023

11

11

Trends in Opioid Prescribing for Pain



Racial Differences

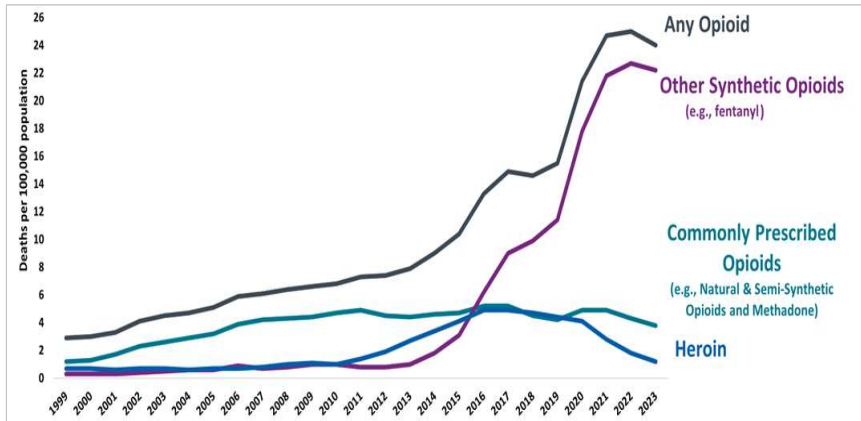
Compared to White patients, Black and Hispanic patients are less likely to receive opioid analgesics for pain and when they do it is at a lower dose

www.fda.gov
Morden NE, et al. *NEJM* 2021

12

12

Trends in Opioid Overdose Deaths



Racial Differences

- Whites had early periods of acceleration 1999-2016 with decrease rate of change starting in 2016
- American Indian/ Alaska Native and non-Hispanic Black persons experienced the highest increases in drug overdose death rates starting in 2019

Furr-Holden D, et al. *Addiction*. 2020

Kariisa M, et al. *MMWR*. 2022

Spencer MR et al. *National Center for Health Statistics*. 2024

13

13



Part 1: Understanding Pain and Opioids

14

14

Case Study - Michelle Jones

Medical History

- 36-year-old female with no past medical history
- Displaced right femoral neck fracture after a motor vehicle crash
- Underwent internal fixation
- Perioperative pain managed with nerve blocks and parenteral hydromorphone



15

15

Assessing Acute Pain

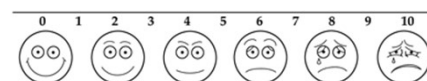
S	Site
O	Onset
C	Character
R	Radiation
A	Associations
T	Time course
E	Exacerbating/relieving factors
S	Severity

"Many factors influence self-reported pain including gender, social support, clinician characteristics, trust."

~ Barry S. Oken, MD, PhD

Pain intensity scales include:

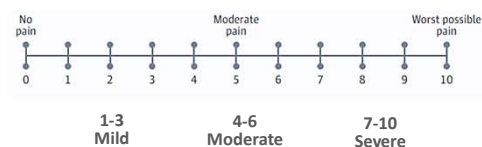
- Visual Analogue Scales (VAS)



- Emoji-based VAS



- Numerical Rating Scales (NRS) 10-point scale



He S, et al. *JAMA*. 2022
 Oken BS. *Brain*. 2008
 Breivik H, et al. *Br J Anaesth*. 2008
 Mason ST, et al. *Handbook of Pain Assessment*. 2011

16

16

Risk Factors: Developing Chronic Postsurgical Pain

Alterations in expression of neurotransmitters, receptors, and ion channels
Changes to neuron structure, connectivity, and survival

Patient-related

- Younger
- Female
- History of
 - Anxiety
 - Depression
 - Catastrophizing
 - Pre-existing pain syndrome
 - Preoperative opioid use

Persistent Pain

Intraoperative variables

- Surgical procedure
- Nerve ligation/injury
- Ischemia

Postoperative pain

- Uncontrolled high intensity pain
- Longer duration of postoperative pain

Voscopoulos C, Lema M. *Br J Anaesth*. 2010
Pozek JP, et al. *Med Clin North Am*. 2016

17

17

Risk: Acute to Chronic Musculoskeletal Pain STarT MSK Screening Tool

- Helps identify **modifiable risk factors** (biomedical, psychological, social) **for chronic musculoskeletal pain disability**
- Score stratifies risk:
 - Low (0-3)
 - Medium (4-7)
 - High (8-9)

Pain Characteristics

Catastrophizing

Last 2 weeks...(disagree [0] or agree [1])

1. ...troublesome joint or muscle pain in more than one part of your body?
2. ...only been able to walk short distances because of your pain?
3. ...dress more slowly than usual because of your pain?
4. ...other important health problems?
5. ...feel it is unsafe...to be physically active?
6. ...worrying thoughts about your pain a lot of the time?
7. ...your pain condition will last a long time?
8. ... stopped enjoying all the things you usually enjoy?
9. How bothersome has your pain been...
(not at all, slightly, moderately, very much, extremely)

Campbell P, et al. *J Pain Res*. 2016

18

18

Case Study - Michelle Jones



What is the correct amount of opioid to discharge this patient on?



Discharged Home

- Visiting nurse and home physical therapy
- Orthopedic follow-up in 1 week
- Received prescriptions for
- Ibuprofen 600 mg every 8 hours prn pain
- Oxycodone (5 mg) 1-2 tablets every 4-6 hours prn pain (#40 tablets)



19

19

Opioid Overprescribing for Acute Pain



Overprescribing

- Postoperatively over 70% of patients took half or less of their opioids
- After ED visit (e.g., renal colic, fracture/dislocation) 93% of patients had leftover pills, 52% of pills were unused

Overprescribing Risk

- Source of prescription opioids misused: 39% family & friends, 44% single prescriber
- 3-5% of opioid-naïve patients receiving an opioid became long-term (>3 months) opioid users (*risk factors: male, over 50, mental illness, substance use disorder*)

Since 2012 there has been a decrease in new opioid prescriptions for more than 7-day supply

Bartels et al. *Plos One*. 2016
Rodgers et al. *J Hand Surg*. 2012

SAMHSA. (2023). 2022 NSDUH
Sun EC, et al. *JAMA Intern Med*. 2016
McCarthy DM, et al. *Pain Med*. 2021

Riva JJ, et al. *Ann Intern Med*. 2020
Deyo RA, et al. *J Gen Intern Med*. 2017
Zhu W et al. *N Engl J Med*. 2019

20

20

Treating Acute Pain

Acute Dental Pain

Molar extractions:
NSAID + APAP more effective compared to oxycodone alone or in combination with APAP

Acute Musculoskeletal Pain

No significant difference in pain reduction with opioids versus NSAID + APAP or different opioid + APAP combinations

Acute Pain Guidelines

Multimodal, individualized approach

Some minor surgeries, appropriate to d/c patients w/ NSAIDs +/- APAP or limited opioids before transition to NSAIDs +/- APAP

CDC Recommendations 1 & 6

- Acute pain: maximize non-pharm and non-opioids
- Only consider opioids if benefits > risks
- Discuss realistic benefits and known risks
- Prescribe no greater quantity than needed for expected duration of severe pain

Dowell D, et al. *MMWR*. 2022

Moore RA, et al. *Cochrane Library* 2015
Chang AK, et al. *JAMA* 2017
Jones CMP, et al. *Lancet* 2023

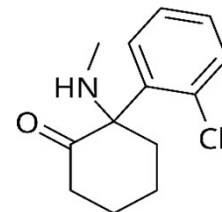
Chou R, et al. *J Pain*. 2016
Qaseem A, et al. *Ann Intern Med* 2020
Fiore JF, et al. *Lancet* 2022

21

21

Ketamine for Acute Pain

- Developed in the 1960s as a dissociative anesthetic
 - Subanesthetic doses for treatment of perioperative, neuropathic and nociceptive pain, and depression and substance use disorders
 - Analgesic without respiratory depression
- Increased parenteral use (IV, IM) as analgesic in ED and perioperative settings
 - Low dose (0.3-0.5 mg/kg) safely reduces pain more rapidly but less sustained than morphine
 - Decreases opioid requirements (“opioid-sparing”)
- Low oral bioavailability and limited evidence for outpatient treatment of chronic pain
 - Outpatient use (e.g., intranasal) is complex due to administration and monitoring requirements
- Dose-dependent adverse effects - hallucinations, agitation, anxiety, dysphoria, euphoria
- Misuse potential due to psychoactive effects



Bell RF, Kalso EA. *Pain Rep*. 2018
Schwenk ES et al. *Curr Pain Headache Rep*. 2021
Guo J, et al. *Am J Emerg Med*. 2024

22

22

Case Study - Michelle Jones - 54 yo female



18 Years Later...

- Presents for primary care, at age 54, after her previous PCP retired
- Chief complaint: **"I need my pain med refilled today. My feet and hip are killing me!"**
- Past medical history:
 - Type 2 diabetes mellitus (A1C 7 %)
 - Painful diabetic neuropathy
 - Diabetic nephropathy (Cr 1.44, GFR 40)
 - Hypertension
 - Hyperlipidemia
 - Obesity (BMI 32)
 - Post-traumatic osteoarthritis of right hip

23

23

Case Study - Michelle Jones - 54 yo female



Current Medications

Metformin, Empagliflozin,
Lisinopril, Atorvastatin

Current Pain Medications

Oxycodone 10 mg 4x/day (60 MME*)
Gabapentin 300 mg 3x/day

Previous Pain Medications

NSAIDs (ibuprofen, naproxen)	<i>Diabetic nephropathy and GI upset</i>
Acetaminophen	<i>Inadequate pain relief</i>
Tricyclic antidepressants (TCA) (amitriptyline)	<i>Inadequate pain relief and dry mouth</i>
Serotonin-norepinephrine reuptake inhibitor (SNRI) (venlafaxine)	<i>Unable to tolerate due to nausea and dizziness</i>
Tramadol	<i>Inadequate pain relief</i>
Acetaminophen with codeine	<i>Inadequate pain relief and nausea</i>

*Morphine Milligram Equivalents

24

24

Case Study - Michelle Jones - 54 yo female



Social History

Paralegal law office 20 hours/week

Married, no children

Substance Use History

No tobacco use

Alcohol use: 1 glass of wine on special occasions

No illicit drug or cannabis use

Family History

Father being treated for lung cancer

Mother died from complications of alcohol-associated cirrhosis

25

25

Case Study - Michelle Jones - 54 yo female



Pain Medications

- Spacing out oxycodone to avoid running out
- Took last oxycodone this morning
- Best pain relief with oxycodone 10 mg every 6 hours
- Current pain is more severe due to less frequent oxycodone
 - “My pain pills don’t last. I’m suffering. It’s almost impossible to go to work.”
- Presents with some medical records from previous PCP

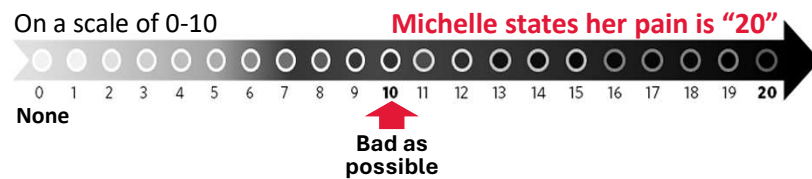
26

26

Case Study - Michelle Jones - 54 yo female

Pain Assessment

- **Moderate right hip pain**
 - Constant deep, aching pain radiating to the right groin
 - Exacerbated with activity and relieved with rest
- **Severe bilateral foot pain**
 - Burning, numbness and tingling
 - Pain worse at night, trouble sleeping because of pain



27

27

Building Trust: Patient Issues

Patients may assume that you do not believe the severity of their pain complaints



Demonstrated by
exaggerating pain scores
and
exaggerating functional limitations

28

28

Building Trust: Clinician Issues

After completing a thorough pain hx, focused exam, and appropriate diagnostic testing...

Show empathy for the patient's experience...empathy is associated with better outcomes among patients with chronic pain*

"I can't imagine how difficult this is for you."

"It must be really hard to live with pain like this."

Validate that you believe the patient's pain and suffering is real...

"Your pain is real."

"Please know that your pain matters and we'll work together to find you relief."

Believing the severity of a patient's pain complaint
does not mean opioids are indicated

*Licciardone JC et al. *JAMA Network Open*. 2024

29

29

Chronic Pain Assessment



Unidimensional Scales

- ☐ (e.g., Numeric rating) are of limited value for assessing chronic pain

Multidimensional Instruments

- ☐ McGill Pain Questionnaire
 - ☐ Graded Chronic Pain Scale
 - ☐ Brief Pain Inventory
- } Impractical for use in most primary care settings

Brief Multidimensional Tool

Pain, Enjoyment, General Activity (PEG) Scale

1. What number best describes your <u>pain on average</u> in the past week:										
0	1	2	3	4	5	6	7	8	9	10
No pain					Pain as bad as you can imagine					
2. What number best describes how, during the past week, pain has interfered with your <u>enjoyment of life</u> ?										
0	1	2	3	4	5	6	7	8	9	10
Does not interfere					Completely interferes					
3. What number best describes how, during the past week, pain has interfered with your <u>general activity</u> ?										
0	1	2	3	4	5	6	7	8	9	10
Does not interfere					Completely interferes					

Breivik H, et al. *Br J Anaesth*. 2008
Salaffi F, et al. *Best Pract Res Clin Rheumatol*. 2015

Krebs EE, et al. *J Gen Intern Med*. 2009

30

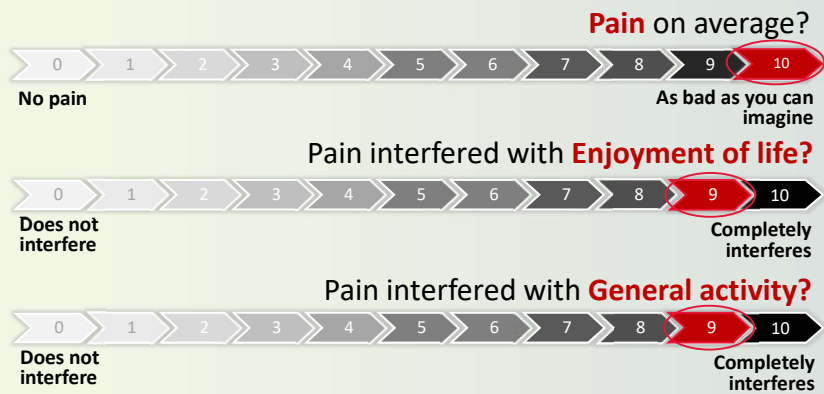
30

Case Study - Michelle Jones - 54 yo female



In the past week...

PEG Scale Assessment



31

31

Case Study - Michelle Jones - 54 yo female



How will you manage this patient's chronic pain?



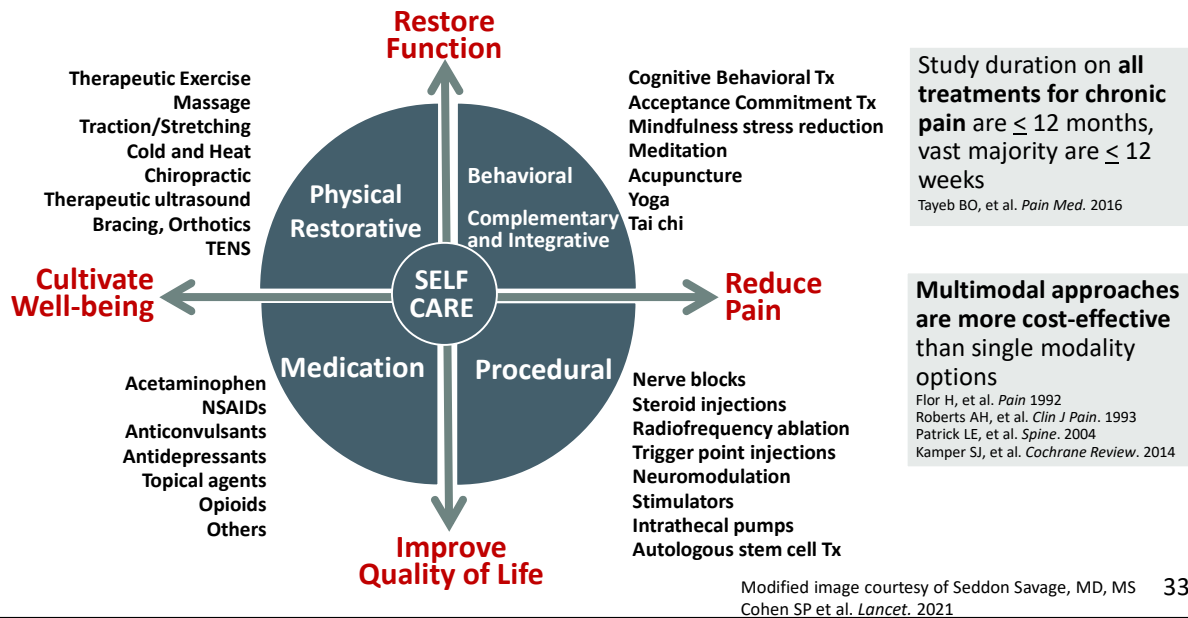
Physical Examination

- No acute distress
- Normal vitals, weight 193 lbs (BMI 32)
- Musculoskeletal exam normal except right hip with decreased internal rotation
- Neurologic exam normal except absent Achilles tendon reflex bilaterally
- Diabetic foot exam:
 - No lesions, normal pulses
 - Loss of protective sensation by monofilament test

32

32

Multidimensional Approach for Chronic Pain



33

Getting Help from a Pain Specialist



- **Know the services** your pain specialist offers
- **Set patient expectations**
 - Let them know what to expect (e.g., full assessment)
 - Never send them with the expectation of a specific treatment (e.g., "I am here for my injection") as this sets up patients for disappointment and frustration
- **Know local or state requirements** requiring pain specialist consultation

Wang VC, Mullally WJ. *Am J Med.* 2020
Slietzky M et al. *J Pain Res.* 2024

34

34

Non-Opioid Pharmacotherapies

Salicylates, Nonacetylated Salicylates

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

- Nonselective and selective COX-2 inhibitor (celecoxib)
- Anti-inflammatory, analgesic, antipyretic

Acetaminophen (APAP)

- Analgesic, antipyretic
- Less effective than full dose NSAIDs in relieving chronic pain but fewer adverse effects

General Considerations

- Ceiling analgesic effects
- No known analgesic tolerance
- Additive role (NSAID+APAP)
- Some patients may respond better to one NSAID than another
- Side effects (GI, renal, CV) especially at high NSAID doses

Med Lett Drugs Ther. 2022
Finnerup NB. *N Eng J Med.* 2019

35

35

Non-Opioid Pharmacotherapies

- Analgesics with primary indication other than pain

- **Antidepressants** (TCAs, SNRIs)
- **Anticonvulsants** (gabapentinoids, carbamazepine)
- **Antispasmodics/muscle relaxants**
- **Local anesthetics** (lidocaine)

} Mainstay of pharmacologic treatments for neuropathic and nociplastic pain syndromes



Caution:

- Misuse and addiction potential with:
 - Gabapentinoids (gabapentin, pregabalin)
 - Muscle relaxants (carisoprodol metabolizes into meprobamate (barbiturate-like drug))
- Additive burden of anticholinergic side effects (e.g., TCAs, cyclobenzaprine)

Med Lett Drugs Ther. 2022
Finnerup NB. *N Eng J Med.* 2019
Evoy KE et al. *Drugs.* 2021
Hill J, Alford DP. *Semin Neurol.* 2018

36

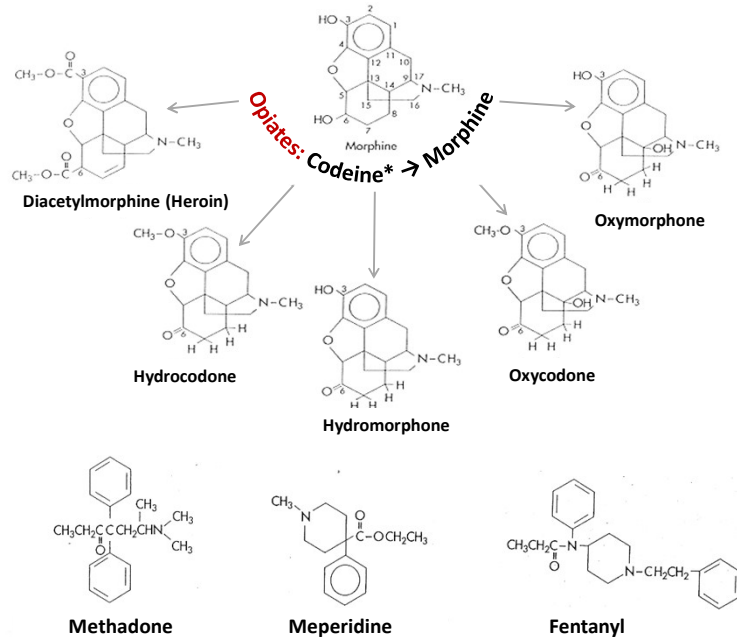
36

Opioids

Natural (Opiates)

Semisynthetic

Synthetic



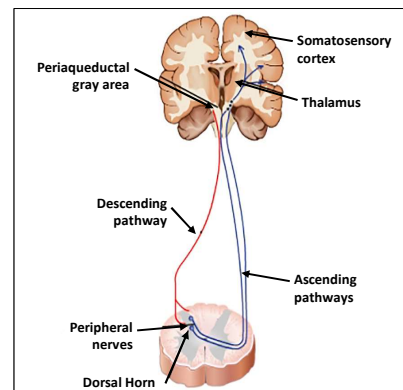
* Codeine is a prodrug of morphine

37

37

Opioid Analgesics

- Turn on descending inhibitory systems
- Prevent ascending transmission of pain signal
- Inhibit terminals of C-fibers in spinal cord
- Inhibit activation of peripheral nociceptors
- Responses are variable (not all patients respond to the same opioid in the same way)
 - >3,000 polymorphisms in human μ opioid receptor gene
 - Single nucleotide polymorphisms (SNPs) affect opioid metabolism, transport across the blood brain barrier, and activity at receptors and ion channels
- **Activate the reward pathway**



(ScienceMedia.com), Acute versus Chronic pain and Pain Pathways, Nov 2019.

McCleane G, Smith HS. *Med Clin N Am*. 2007. Smith HS. *Pain Physician*. 2008. Ren Z et al. *Pain Physician*. 2015

38

38

Opioid Tolerance and Physical Dependence

Both tolerance and physical dependence are physiological adaptations to chronic opioid exposure



Tolerance:

- Increased dosage needed to produce specific effect
 - Develops readily for CNS and respiratory depression
 - Less so for constipation
 - **Unclear about analgesia**



Physical Dependence:

- Signs and symptoms of withdrawal by abrupt opioid cessation, rapid dose reduction or exposure to an opioid antagonist (naloxone)

39

39



Opioid Efficacy and Safety



40

40

Opioid Efficacy for Chronic Pain



Meta-analyses (3-6 m f/u)

- **Opioids vs placebo**
(*high quality studies*)
Opioids with statistically significant, but small, improvements in pain^{1,2} and physical functioning²
- **Opioids vs nonopioids**
(*low-mod quality studies*)
Similar benefits²

RCT³ found opioids **not superior** to nonopioids for improving musculoskeletal pain-related function over 12 months

*Limitations to generalizability:*⁴

- Excluded patients already on long-term opioids

Two longer term follow-up studies found **44.3%** on chronic opioids for chronic pain had **at least 50% pain relief**⁵

1. Meske DS, et al. *J Pain Res.* 2018
2. Busse JW, et al. *JAMA.* 2018

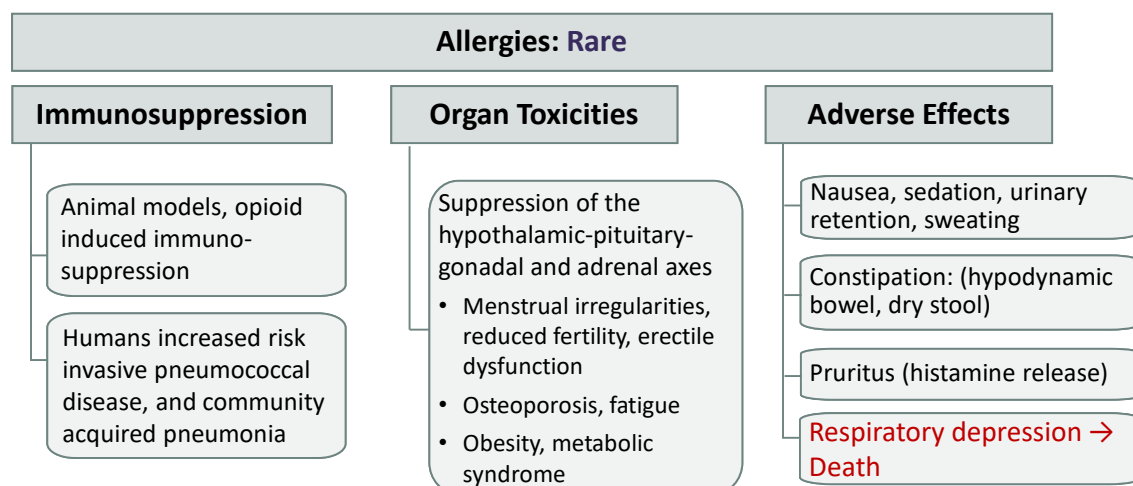
3. Krebs EE, et al. *JAMA.* 2018
4. Webster L. *Pain Med.* 2019

5. Noble M, et al. *Cochrane Syst Rev.* 2010

41

41

Opioid Safety and Risks



Diasso PD, et al. *Eur J Pain.* 2019
Wiese AD, et al. *Ann Intern Med.* 2018
Edelman EJ, et al. *JAMA Intern Med.* 2019
Sharma P, et al. *J Soc. Health Diabetes.* 2016

Report AE to FDA 1-800-FDA-1088, www.fda.gov

42

42

Managing Opioid Adverse Effects

Nausea and Vomiting

- Usually resolves in a few days
- Antiemetics, switch opioids

Sedation

Mostly during initiation or change in dose

- **Decrease dose**

Constipation

Most common and should be anticipated

- Stool softeners, osmotic stimulants
- Peripherally-acting opioid antagonists
- Switch opioids, avoid bulking agents

Pruritus

- Switch opioids
- Antihistamines

Urinary Retention

- Switch opioids

Paul AK, et al. *Pharmaceuticals*. 2021
Hanson B et al. *Gastroenterology*. 2019

43

43

Opioids and Patient Considerations

• Age



- Decline in therapeutic index
- Predisposition to adverse drug effects
- Fall risk, worsening cognitive function

• Medical Co-morbidities



- **Liver disease:** decreased opioid clearance
 - When using morphine, oxycodone, hydromorphone: reduce doses and prolong dosing intervals



- **Kidney disease:** decreased opioid excretion
 - Preferred are hydromorphone, fentanyl, buprenorphine, methadone
 - Oxycodone 2nd line, due to active metabolites
 - Morphine, codeine not recommended due to active metabolites

44

44

Opioids: Drug-Drug Interactions (DDI)

- Mechanism includes inhibition or induction of **cytochrome P450** (CYP450)
 - **Opioids metabolized by CYP450:** numerous DDIs that can reduce or increase opioid effects (e.g., codeine, oxycodone, hydrocodone, fentanyl, tramadol, methadone)
 - **Opioids not metabolized by CYP450:** fewer DDIs (e.g., morphine, hydromorphone)
 - Helpful resource: <http://dailymed.nlm.nih.gov/dailymed>
- CNS depressants (benzodiazepines, alcohol, cannabis, other sedatives, hypnotics, TCAs, MAOI) may potentiate opioid effect on sedation and respiratory depression
- Alcohol may rapidly release opioid (dose dump) or increase drug levels w/out dose dumping
- Opioids can reduce efficacy of diuretics by inducing release of antidiuretic hormone



Recommendation 11

Use caution when concurrently prescribing opioids and benzodiazepines (and other CNS depressants)

Dowell D, et al. MMWR. 2022

Kotlinska-Lemieszek A, et al. *Drug Des Devel Ther.* 2015.

45

45

Problematic Opioid Use in Chronic Pain

Systematic review of 38 studies
(26% primary care, 58% pain clinics)

Misuse rates: 21% - 29%

(95%CI: 13%-38%)

Misuse: Use contrary to the prescribed use, regardless of the presence or absence of harm or adverse effects

Addiction rates: 8% - 12%

(95% CI: 3%-17%)

Addiction: Pattern of continued use with experience of, or potential for, harm

Vowles KE, et al. *Pain.* 2015

46

46

Collateral Opioid Risk



Risks

- Young children's ingestion and overdose*
- Adolescent experimentation leading to overdose and addiction
- Other household contacts (family, visitors)

Mitigating risk

- Safe storage (e.g., lock box)
- Child resistant packaging
- Mail-back envelopes: As of 3/2025, REMS Program Companies are required to provide pre-paid drug mail-back envelopes upon request to pharmacies and other dispensers of opioid analgesics.
- Safe disposal www.deadiversion.usdoj.gov/drug_disposal/
- Opioid overdose education and naloxone distribution**
 - More information: www.prescribetoprevent.org



Recommendation 8

Use strategies to mitigate risk including naloxone co-prescribing

Dowell D, et al. MMWR. 2022

* Gaither JR, et al. JAMA Pediatr. 2016

** Beletsky L, Rich JD, Walley AY. JAMA 2012

** SAMHSA Opioid Overdose Prevention Toolkit 2018

47

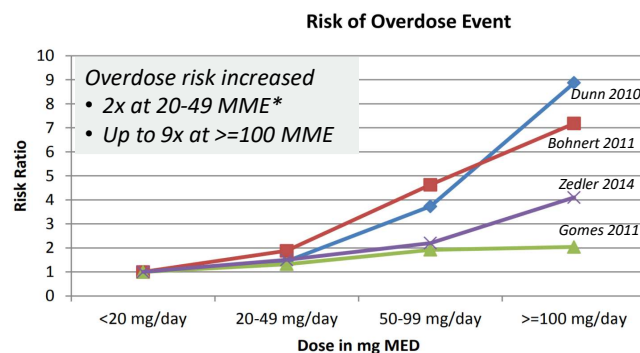
47

Higher Dose Opioids

A lack of high-quality evidence about the efficacy of high-dose opioids for chronic pain

Higher doses associated w/:

- Immunosuppression
- Hyperalgesia
- Reduced function
- **Overdose risk**



*MME: Morphine Mg Equivalent

Els C, et al. Cochrane Reviews 2023

Kobus AM, et al. J Pain. 2012

Huxtable CA, et al. Anaesth Intensive Care. 2011

Brush DE. J Med Toxicol. 2012

Lee M, et al. Pain Physician. 2011

Braden JB. Arch Intern Med. 2010

Paulozzi LJ. Pain Med. 2012

Edelman EJ, et al. JAMA Int Med. 2019

Dunn KM, et al. Ann Intern Med. 2010

Bohnert AS, et al. JAMA. 2011

Zedler B et al. Pain Med. 2014

Gomes T, et al. Open Med. 2011

48

48

Higher Dose Opioids

Patient on high doses...

- Manage as higher risk
- Increase monitoring and support



Recommendation 4

- When starting opioids, prescribe lowest effective dosage
- Use caution at any dosage
- Carefully evaluate benefits and risks when considering increasing dosage
- Avoid increasing dosage above levels with diminishing benefit relative to risk

Dowell D, et al. MMWR. 2022

49

49



Risk Factors



50

50

Risk Factors for Opioid-Related Harm

(misuse, overdose, addiction)



Medication Factors

Higher opioid dose

Long-term opioid use (>3 months)

Extended release/long-acting (ER/LA) opioid

Initial 2 weeks after starting ER/LA opioid

Combination opioids and sedatives (e.g., benzodiazepines)

Patient Factors

Mental health disorder (e.g., depression, anxiety)

Substance use disorder (SUD) (e.g., alcohol, tobacco, illicit and prescription drug)

Family history of SUD

History of opioid overdose

Sleep-disordered breathing

Akbik H, et al. *J Pain Symptom Manage.* 2006
Ives J, et al. *BMC Health Serv Res.* 2006
Liebschutz JM, et al. *J Pain.* 2010

Michna E, et al. *J Pain Symptom Manage.* 2004
Reid MC, et al. *J Gen Intern Med.* 2002
Volkow ND, et al. *N Engl J Med.* 2016

51

51

Screening for Sleep-Disordered Breathing

STOP-BANG Questionnaire

STOP

Do you **SNORE** loudly?

Do you often feel **TIRED**, fatigued, or sleepy during daytime?

Has anyone **OBSERVED** you stop breathing during your sleep?

Do you have or are you being treated for high blood **PRESSURE**?

BANG

BMI more than 35?

AGE over 50?

NECK circumference (males: 17+ inches; females: 16+ inches)?

GENDER male?



Sleep Apnea Risk	Total Score
High Risk	5-8
Intermediate Risk	3-4
Low Risk	0-2

Chung F et al. *Anesthesiology* 2008; Chung F et al. *Br J Anaesth* 2012; Chung F et al. *J Clin Sleep Med* 2014.

52

52

Psychiatric Co-Morbidities

- Almost every psychiatric diagnosis in the DSM-5 is also associated with increased rates of chronic pain

- | | |
|--------------------------------|--------------------------|
| • Major depressive disorder | • Sleep disorder |
| • Generalized anxiety disorder | • PTSD |
| • Personality disorder | • Substance use disorder |



- Bidirectional relationship
 - Psychiatric conditions make pain worse
 - Pain makes psychiatric conditions worse
- Should assess for psychiatric conditions and attempt to co-manage

Johnston KJA, Huckins LM. *Complex Psychiatry*. 2023

53

53

Brief Screenings for Co-Morbidities

Depression	➔	PHQ-2 (Patient Health Questionnaire), 2-items
Anxiety	➔	GAD-2 (Generalized Anxiety Disorder), 2-items
PTSD	➔	PC-PTSD-5 (Primary Care PTSD Screen for DSM-5), 5-items
Sleep Disorder	➔	ISI-3 Insomnia Severity Index, 3-items
Suicidality	➔	ASQ (Ask Suicide-Screening Questions), 4-items

Kroenke K, et al. *Med Care*. 2003
 Kroenke K, et al. *Ann Intern Med*. 2007
 Prins A, et al. *J Gen Intern Med*. 2016
 Thakral M, et al. *Sleep Med*. 2021
 Horowitz LM, et al. *Psychosomatics*. 2020

54

54

Screening for Substance Use

TAPS (Tobacco, Alcohol, Prescription Medication, and Other Substance Use) Tool

In the PAST 12 MONTHS, how often have you...

...used tobacco or any other nicotine (i.e., e-cigarette, vaping or chewing tobacco)?

...had **5 or more** drinks (men)/**4 or more** drinks (women) containing alcohol in one day?

...used any prescription medications just for the feeling, more than prescribed or that were not prescribed for you?

...used any drugs including marijuana, cocaine or crack, heroin, methamphetamine (crystal meth), hallucinogens, ecstasy/MDMA?

McNeely J, et al. *Ann Intern Med.* 2016

55

55

Case Study - Michelle Jones - 54 yo female



**Will you prescribe
opioids?**



Screening Results

- Negative for sleep-disordered breathing
- Negative for insomnia, depression, and anxiety
- Negative for unhealthy substance use

56

56

When Are Opioids Indicated?

- Pain is severe
- Pain has significant impact on function and quality of life
- Pain type potentially opioid-responsive
nociceptive or neuropathic pain
but less so for nociplastic pain and headache syndromes (e.g., migraines)
- Inadequate benefit from non-opioid modalities
- If already on opioids, is there documented benefit (pain, function, quality of life)?

57

57

Opioids and Chronic Pain in Perspective

The efficacy of **long-term opioid therapy** for chronic pain has been **inadequately studied**

- Opioid prescribing should be more judicious
- Opioid misuse can be fatal (overdose, addiction)
- Opioids for chronic pain...
 - Are indicated after alternative safer options are inadequate
 - Are only one tool of a multimodal approach for managing severe chronic pain



Recommendation 2

- Maximize non-pharmacologic and non-opioid therapies
- Only consider opioids if expected benefits (pain/function) > risks
- Before starting opioids discuss realistic benefits and known risks
- Establish treatment goals and how opioids will be discontinued if benefits < risks

Dowell D, et al. MMWR. 2022

Chou R, et al. *Ann Intern Med.* 2015
 Dowell D, et al. *JAMA.* 2016
 Manchikanti L, et al. *Pain Physician.* 2011
 Reuben DB, et al. *Ann Intern Med.* 2015
 Volkow ND, McLellan T. *N Engl J Med.* 2016

58

58

Patients on Opioid Therapy from Previous Clinician “Legacy Patients” “Opioid Orphans”

- Review the patient history with the former clinician, if possible
- Review prescription history (e.g., Prescription Drug Monitoring Program)
- Assess the patient for opioid use disorder and treat or refer to specialty care, if indicated
- Consider a therapeutic bridge for the patient until a plan of care is determined given the risks associated with stopping opioid therapy abruptly
- Document rationale for treatment plan and next steps

Coffin PO, et al. *N Engl J Med*. 2022



Recommendation 5

For patients already on opioids, carefully weigh benefits and risks

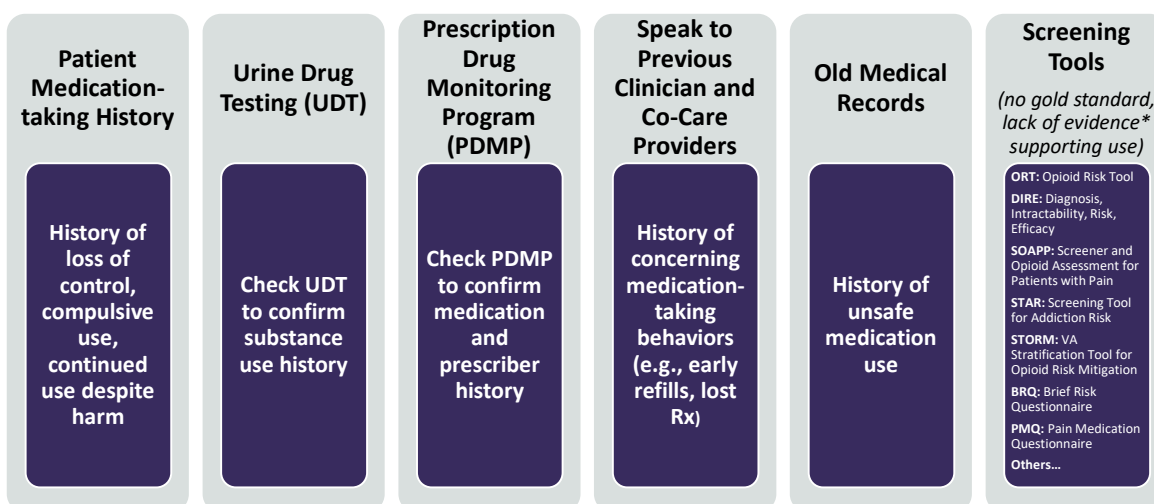
- If benefits > risks, continue opioids and optimize other therapies
- If risks > benefits, optimize other therapies, gradually taper opioids to lower dosages
- Unless life-threatening issue (i.e., impending overdose), do not abruptly reduce opioids from higher dosages

Dowell D, et al. *MMWR*. 2022

59

59

Assess for Opioid Misuse Risk Prior to Prescribing



Moore TM, et al. *Pain Med*. 2009
*Klimas J et al. *JAMA Network Open*. 2019

60

60

Case Study - Michelle Jones - 54 yo female

PDMP showed
oxycodone 10 mg
#120 tablets per
month with one
prescriber and one
pharmacy, last filled 7
weeks ago



At 1st visit

- Prescribed oxycodone 10 mg 4x/day x 2 weeks (#56)
- Continued gabapentin 300 mg 3x/day
- Added acetaminophen 500 mg 4x/day
- Sent urine drug test (UDT)
- Obtained release to contact previous PCP

Before 2nd visit

- Reviewed previous medical records
 - Problem and medication lists reconciled
 - Inadequate documentation about benefits (e.g., pain, function) or monitoring (e.g., UDT) BUT no evidence of worrisome behaviors (e.g., early refills)

61

61

Questions for Next Visit



Clinician Concerns:

- Should I change the opioid dose?
- Should I change to an ER/LA opioid?
- What about any other adjuvant medications or therapies?
- What sort of treatment plan should I develop?

62

62

Summary Part 1



Opioids...

- Should not be first line treatment option
- Are just one tool in a multimodal approach
- Side effects are common and can be managed
- Carry significant risk including addiction, overdose, death
- Misuse risk can be assessed using systematic approach which includes screening for co-morbidities

63



1



2

Case Study - Michelle Jones - 54 yo female



Should opioids be continued?

If so, should the opioid be changed?



In the interim...

- Unable to contact previous PCP who retired
- UDT positive for oxycodone only (as expected)

Office Visit 2

- PEG scores:
 - “6 out of 10” after oxycodone dose
 - “9 out of 10” right before next oxycodone dose
- Denied sedation
- Completed 2-week oxycodone prescription on schedule

3

3

Opioid Choices

Immediate Release/ Short-acting (IR/SA)

- Morphine
- Hydrocodone
- Hydromorphone
- Oxycodone
- Oxymorphone
- Tramadol
- Tapentadol
- Buprenorphine (buccal)
- Fentanyl (transmucosal)
- Codeine

Extended Release/ Long-acting (ER/LA)

- Morphine
- Hydrocodone
- Hydromorphone
- Oxycodone
- Oxymorphone
- Tramadol
- Tapentadol
- Buprenorphine (transdermal)
- Fentanyl (transdermal)
- Methadone

Product-specific information: <http://dailymed.nlm.nih.gov/dailymed>; pharmacy medication guide; www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass

4

4

Choosing IR/SA vs ER/LA Opioids



IR/SA Opioids

- No opioid tolerance/opioid naïve
- Intermittent or occasional pain (PRN dosing)

ER/LA Opioids

- Opioid tolerance exists
- Constant, severe, around-the-clock pain (scheduled dosing)
- To stabilize pain relief when patient using multiple doses of IR/SA opioids
- **MUST NOT be broken, chewed or crushed**

Always
start low
and
go slow



Recommendation 3

When starting opioids, use IR instead of ER/LA opioids

Dowell D, et al. MMWR. 2022

Note: No adequate studies of ER/LA opioids in pregnant women; use only if benefit significantly outweighs risk.

5

5

IR/SA vs ER/LA Opioid Uncertainties



Insufficient Evidence

to determine whether
ER/LA opioids are
more effective or safer
than IR/SA opioids

**Individualize
Treatment**

Choose options
that best meet
patient's needs

Debate

whether bolus dosing
(IR/SA) or continuous
exposure (ER/LA) is more
likely to result in
analgesic tolerance,
hyperalgesia or addiction

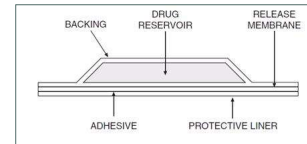
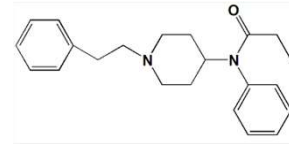
Chou R, et al. *J Pain Symptom Manage.* 2003
Argoff CE, Silvershein DI. *Mayo Clin Proc.* 2009

6

6

Transdermal Fentanyl

- Dosed in micrograms (mcg)
- Slow peak onset (>24-72h)
- Delayed offset (serum $t_{1/2}$ life >17-26h)
- Sustained release requires predictable blood flow and adequate subcutaneous fat
- Absorption increased with fever or broken skin
- Absorption decreased with edema
- Some with metal foil backing not compatible with MRI



Fentanyl

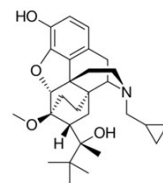
- Every 72 hours
- Dosages (mcg/hr): 12, 25, 37.5, 50, 62.5, 75, 87.5, 100

7

7

Buprenorphine

- Partial opioid agonist
- Formulations approved for treatment of pain or opioid use disorder (OUD)
- Precipitates opioid withdrawal if initiated while full opioid agonist highly bound



Pain (dosed in mcg)

- Taper prior opioid to <30 MME before starting buprenorphine

Buccal film 75-900 mcg q12-24

- Do not cut, chew or swallow

Transdermal patch 5-20 mcg/hr q 7 days

- (mcg/hr): 5, 7.5, 10, 15, 20 (max)
- Rotate sites wait min 3 wks before using same site

OUD (dosed in mg)

- Some formulations contain naloxone
- Induction procedure to avoid precipitating opioid withdrawal (www.samhsa.gov/sites/default/files/quick-start-guide.pdf)

Sublingual & buccal tablets & film (8-32 mg/d)

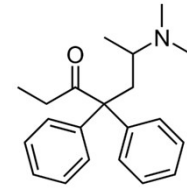
SQ injection:

- Weekly (8-64 mg)
- monthly (64-300 mg)

8

8

Methadone is Complex



- The problem...potentially the most dangerous opioid
- Long, variable, unpredictable half-life
 - Analgesia 6-8 hours while serum $t_{1/2}$ 20-120 hours
- QTc prolongation, risk of torsades de pointes
- Only available in 5 mg & 10 mg tablets leading to large pill burden for patients on higher dosages

Some possible advantages:

- NMDA receptor antagonist
- Potentially less analgesic tolerance, better efficacy in neuropathic pain
- No active metabolites
- Inexpensive, small dosage units (5mg tablets)

Fredheim OM, et al. *Acta Anaesthesiol Scand*. 2008
Chou R, et al. *J Pain*. 2014

9

9

Dual Mechanism Opioids

Norepinephrine and Serotonin reuptake inhibition

Tramadol

Weak μ -opioid receptor agonist
Minimal norepinephrine effect
Prominent serotonin effect

Tapentadol

Stronger μ -opioid receptor agonist
Prominent norepinephrine effect
Minimal serotonin effect

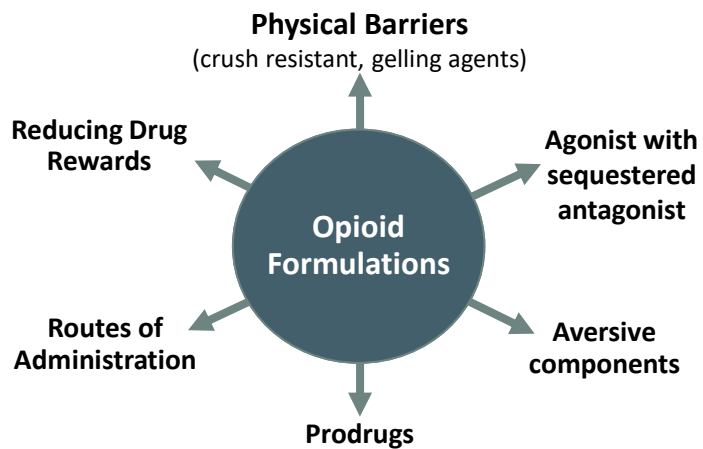


Seizure risk
Physical dependence
Serotonin syndrome
Controlled substances with addiction potential

10

10

Abuse Deterrent/Resistant Formulations



- Decrease medication diversion and street price
- Does not prevent taking many intact tablets
- Are expensive and some insurers do not cover them



Currently, there are **no 100% proven misuse resistant opioids**

Passik SD. *Mayo Clin Proc.* 2009
 Stanos SP, et al. *Mayo Clin Proc.* 2012
 Michna E, et al. *Curr Med Res Opin.* 2014
 Cassidy TA, et al. *Pain Med.* 2014
Medical Letter. June 5, 2017

Updated list of abuse-deterrent opioids: www.fda.gov/drugs/drugsafety

11

11

Additional Considerations



12

12

Opioid Choice Summary

- Duration and onset of action
 - Consider pattern of pain: intermittent vs. constant
- Patient's prior experience (effects & side effects)
 - Mu-opioid receptor polymorphisms and differences in opioid metabolism
- Patient's level of opioid tolerance (always assess before starting ER/LA opioid formulations)
- Age, other medications and diseases
- Route of administration
- Cost and insurance issues

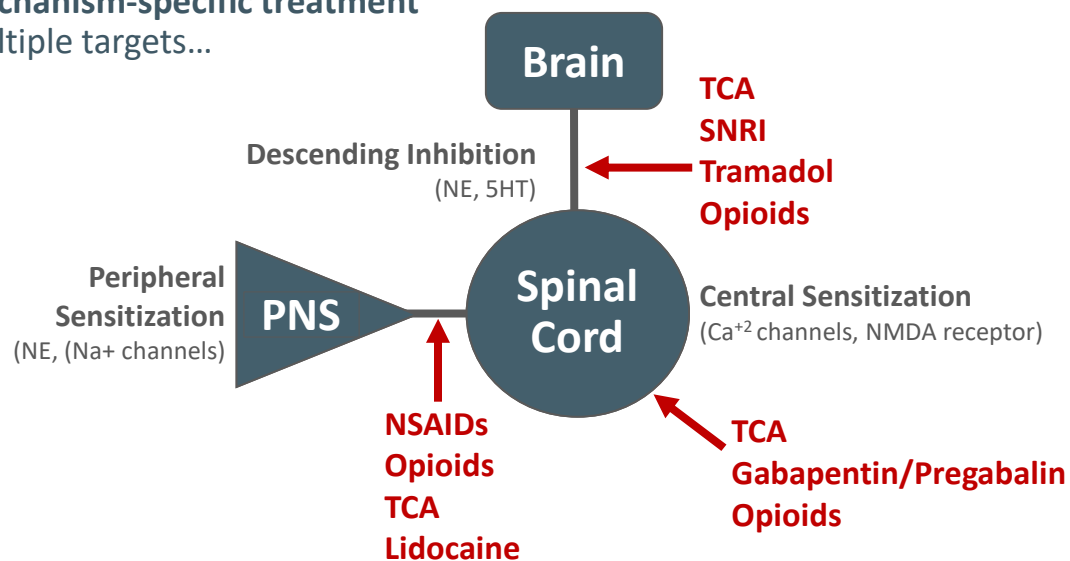


13

13

Rational Polypharmacy

Mechanism-specific treatment
Multiple targets...



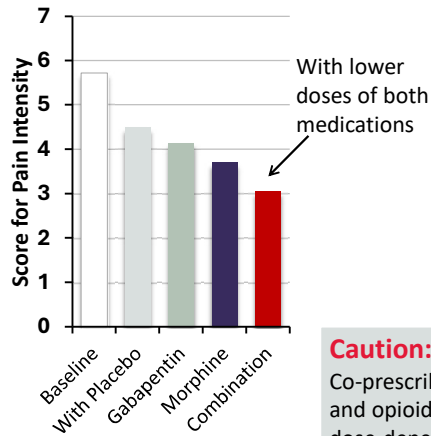
Finnerup NB. *N Eng J Med.* 2019
Woolf CJ. *Ann Intern Med.* 2004

14

14

Exploit Synergism

e.g., Treating painful diabetic neuropathy

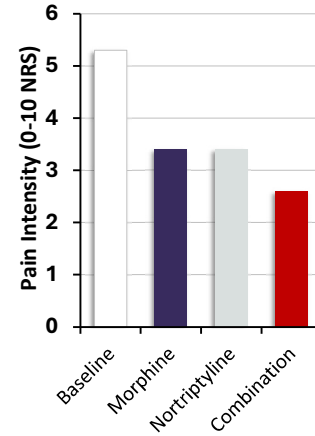


Caution:

Co-prescribing gabapentinoids and opioids is associated with dose-dependent increased risk for opioid-related deaths

Gilron I, et al. *N Engl J Med.* 2005

Gomes T, et al. *Ann Intern Med.* 2018
Goodman WC, Breatt AS. *N Engl J Med.* 2017



Gilron I, et al. *Pain.* 2015

15

15

Case Study - Michelle Jones - 54 yo female

Change Opioid Regimen

- Tolerates IR oxycodone 10 mg 4x/day (60 MME) but...
 - Periodicity of effects (on-off) may be causing inadequate pain control due to “withdrawal-mediated pain”
 - Analgesia may improve with more stable blood levels using ER/LA oxycodone requiring a lower daily dose (15 mg 2x/day) (45 MME)
 - Don’t assume need for breakthrough medication
- Reviewed, signed Patient Provider Agreement (PPA)
- Referred to PT for chronic right hip pain
- Counseled on weight loss



16

16

Universal Precautions when Prescribing Opioids

Predicting opioid risk and misuse is imprecise

Consistent application of precautions reduces stigma and standardizes care

Precautions include:

- Assess and document pain diagnosis(es) and opioid misuse risk
- **Prescribe opioids as a test or trial;** continued, modified or discontinued based on risks/benefits (e.g., every 1-3 months)
- State maximum number of tablets to be taken per day
- Use Patient Prescriber Agreements written at 5th grade level, without coercive language
- Monitor for adherence, misuse, and diversion



Recommendation 7

Evaluate benefits and risks 1-4 weeks of starting opioids or after dose escalation and then regularly

Dowell D, et al. *MMWR*. 2022

Gourlay DL, Heit H. *Pain Med*. 2005 Chou R, et al. *J Pain*. 2009 Franklin GM. *Neurology*. 2014 FSMB 2024 www.fsmb.org/opioids/

17

17

Patient Provider Agreement (PPA)

Informed Consent		Plan of Care
Realistic Goals • Reduce (<i>not eliminate</i>) pain • Improve function (SMART goals): Specific Measurable Action-oriented Realistic Time-sensitive	Potential Risks • Adverse effects and DDI • Over-sedation, impairment (esp. during dose adjustments) • Misuse • Overdose • Death • Risk of neonatal opioid withdrawal • Hyperalgesia • Victimization by others	• Engage in other treatments as directed • Safer opioid use: take as directed, don't double dose if dose missed, safe storage/disposal, no sharing • No illicit drugs, avoid/minimize sedatives • Report other meds, adverse effects • Pregnancy plans • Discuss birth control • Monitor for pregnancy • Discuss risk of neonatal opioid withdrawal • Discuss all opioids transfer into human milk to some degree

Tobin DG, et al. *Cleve Clin J Med*. 2016
 Nicolaidis C. *Pain Med*. 2011
 Paterick TJ, et al. *Mayo Clin Proc*. 2008

Mailis-Gagnon A, et al. *Clin J Pain*. 2012
 Cheatle MD, Savage SR. *J Pain Symp Manage*. 2012
 Tolia VN, et al. *N Engl J Med*. 2015

Schumacher MB, et al. *Psychopharm*. 2017
 Hale TW, Krutsch K. *Clin Pharmacol Ther*. 2021

18

18

Monitoring: Urine Drug Testing

Objective data

- Information on therapeutic adherence
- Information on use of illicit drugs



- Document time of last medication use
- Discuss urine drug testing openly with patient → "If I send your urine now, what will I find in it?"
- Discuss unexpected findings with open-ended questions → "Your urine had 'x' please tell me about it?"
- One medical data point to integrate with others
 - Cannot discriminate elective substance use from substance use disorder or diversion
 - Opioid concentrations cannot determine how much opioid is being taken
- Dedicated deceivers can beat the system

Argoff CE, Alford DP, Fudin J et al. *Pain Med.* 2018
 Nagpal G et al. *JAMA.* 2017
 Christo PJ, et al. *Pain Physician.* 2011



Use strategies to mitigate risk including using toxicology testing

Recommendations 10

Dowell D, et al. *MMWR.* 2022

19

19

Monitoring: Urine Drug Testing

Urine drug screens usually immunoassays

- Quick, inexpensive and can be done at point of care
- Know what is included in your testing panel
- Risk of **false negatives** due to cut offs and **false positives** due to cross reactions

Unexpected findings verified with definitive testing*

- Very specific (identifies specific molecules) but more expensive
- Know opioid metabolism to interpret GC-MS or LC-MS results, for example:
 - hydrocodone → hydromorphone
 - oxycodone → oxymorphone



*Gas Chromatography (GC) or Liquid Chromatography (LC), and Mass Spectroscopy (MS)

Contact lab toxicologist for questions regarding unexpected results

Argoff CE, Alford DP, Fudin J et al. *Pain Med.* 2018
 Reisfield GM, et al. *Bioanalysis.* 2009

20

20

Monitoring: Medication Count and Prescription Drug Monitoring Program (PDMP)

Medication Count

Information on

- Medication adherence
- Possible diversion

28-day (vs 30-day) decreases risk of running out on weekends and medication hoarding



Recommendation 9

Use strategies to mitigate risk including reviewing PDMP data

Dowell D, et al. MMWR. 2022

Fink DS, et al. *Ann Intern Med.* 2018

PDMP

Information on

- Harmful polypharmacy
- Multiple prescribers

Some states:

- require utilization of PDMP
- allow delegating access to others
- have interstate data sharing

Methadone administered or dispensed at addiction treatment programs not routinely included

Insufficient evidence that PDMPs increase or decrease opioid overdoses

21

21

MINIMUM Level of Monitoring Based on Risk

TOPCARE (Transforming Opioid Prescribing in Primary Care) www.opioidresources.org

One example:

Risk Level	Visits (per year)	• UDT • Pill Counts • PDMP (per year)
• ORT: Opioid Risk Tool • DIRE: Diagnosis, Intractability, Risk, Efficacy • SOAPP: Screener & Opioid Assess for Pts w/ Pain		
Low	4	2
Moderate	4	4
High	6	6

- States laws may mandate level of monitoring
- Monitoring more intensive during first 6 months of opioid therapy

Liebschutz JM, et al. *JAMA Intern Med.* 2017

22

22

Monitoring and Documentation: Office Visits

National study, found approximately **30% of charts had no pain diagnosis** at a visit when opioid was prescribed

Six A's

Analgesia

Activities

Adverse effects

A aberrant behaviors

Affect

Adherence

Sherry TB, et al. *Ann Intern Med.* 2018

Passik SD, et al. *Clin Ther.* 2004

Include:

- **Subjective reports** from patient, co-care providers, caregivers and "reliable" family members (beware of those with secondary gain for giving inaccurate information)
- **Objective information** (observations, PEG scores, drug tests, pill counts, PDMP)
- **24-hour inventory** "Tell me how you are taking your medications." "Do you miss doses on some days?" "On average how many doses do you take per day?"

Know federal and state guidelines and regulations: www.deadiversion.usdoj.gov/pubs/manuals/index.html
 Templates in Resources at: www.scopeofpain.org and www.opioidresources.org

23

23

What is the Clinician's Role?

Use a risk-benefit framework

Judge the opioid treatment, not the patient



NOT



Nicolaidis C. *Pain Medicine.* 2011

24

24

Discussing Monitoring

Use a consistent approach

(Universal Precautions)

BUT *apply it individually* to match risk

Review the personal and public/community health risks of opioids

Discuss agreements, pill counts, and drug tests as ways that you are helping to protect patient from getting harmed by medications

Discuss your responsibility to look for and manage early signs of harm

25

25



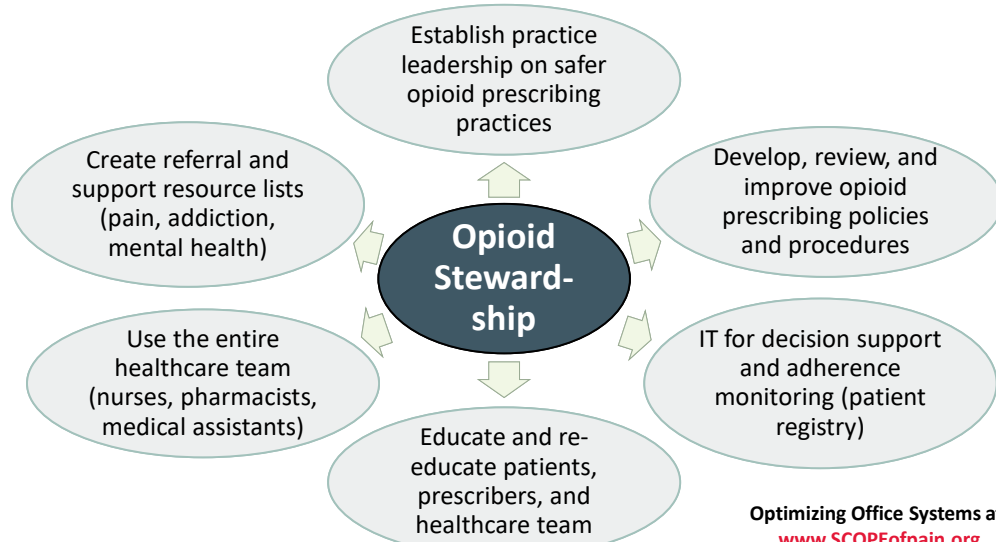
**Safer opioid prescribing
*is a lot of work!***

26

26

Implementing Opioid Stewardship

Prescribing opioids safely, correctly, and under the right circumstances



MacIntyre PE, et al. *JAMA Surg.* 2022

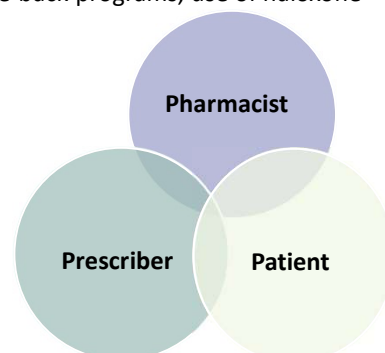
Optimizing Office Systems at:
www.SCOPEofpain.org
 click on: Supplemental Training

27

27

Community Pharmacist

- Must ensure that prescriptions are for “legitimate medical purpose”
- Help with medication choices, doses and substitutions
- Interact with patients
 - Educate on risks, proper use, storage and disposal, drug take-back programs, use of naloxone
 - Check PDMP, monitor for worrisome behaviors
 - Identify potential drug-drug interactions
 - Assist with formularies and prior authorizations
- Prescribers can help by including:
 - Diagnosis or indication on prescription
 - Parameters for when script should be filled
 - Maintain open lines of communication (direct phone lines)



28

28

Case Study - Michelle Jones - 54 yo female

Did well on regimen of ER/LA oxycodone 15 mg bid with gabapentin 300 mg 3x/day for 11 months...



Scenario 1a

- Worrisome opioid taking
- Potential loss of benefit
- Switching opioids

Scenario 2

- Patient requested opioid discontinuation

Scenario 3

- Worrisome opioid taking
- Diagnosing and managing opioid use disorder

Scenario 1b

- Continued lack of benefit after opioid switch
- Clinician initiated opioid discontinuation

29

29

Case Study - Michelle Jones - 54 yo female

Did well on regimen of ER/LA oxycodone 15 mg bid with gabapentin 300 mg 3x/day for 11 months...



Scenario 1a

- Worrisome opioid taking
- Potential loss of benefit
- Switching opioids

Scenario 2

- Patient requested opioid discontinuation

Scenario 3

- Worrisome opioid taking
- Diagnosing and managing opioid use disorder

Scenario 1b

- Continued lack of benefit after opioid switch
- Clinician initiated opioid discontinuation

30

30

Case Study - Michelle Jones - 54 yo female



Scenario 1a

- She then went to the ED of her local hospital, **requesting early refill** of her oxycodone
- ED physician noted that she was in moderate opioid withdrawal and gave her enough ER/LA oxycodone to last until her next PCP appointment in one week
- ED physician left a message with the PCP office regarding patient visit and follow-up plan

31

31

Case Study - Michelle Jones - 54 yo female

Post ED Follow-up



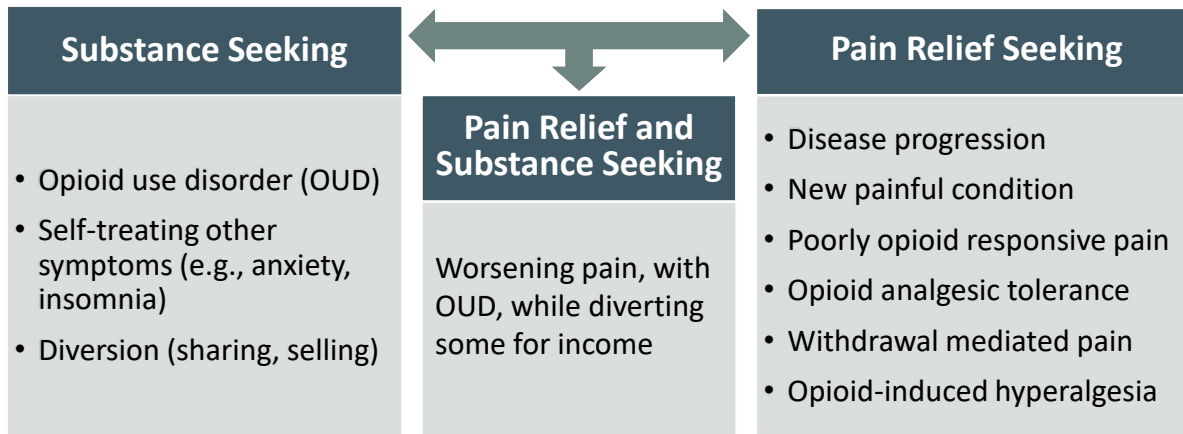
History since last visit

- Foot pain worse in past month "10 out of 10 most days"
- Extra oxycodone in the afternoon and ran out early
- Requests increase in her dose
- Concerned "body has become used to current dose"; doesn't seem to work all day anymore
- Husband says she has become "addicted"
- Difficult to go to work due to severe pain
- She is re-educated about risks including death of self-escalating her opioid dose

32

32

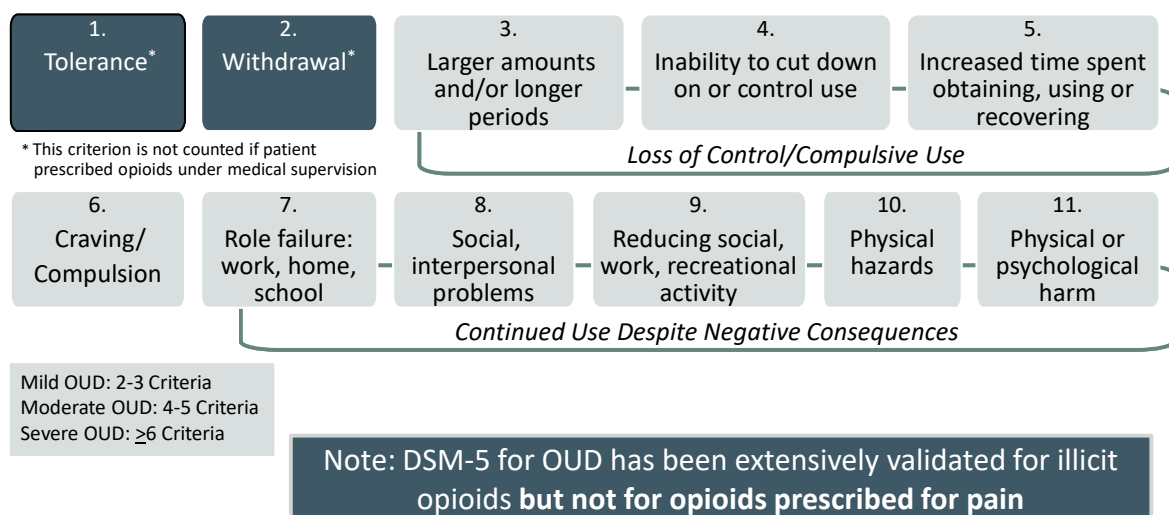
Worrisome Medication-Taking Behaviors: Differential Diagnosis



33

33

DSM-5 Opioid Use Disorders (OUD)



APA. (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.)

Hasin DS, et al. *Am J Psych.* 2022

34

34

Discussing Possible Opioid Use Disorder (OUD)

Give specific, timely feedback about behaviors that raise your concerns for possible OUD (e.g., loss of control, compulsive use, continued use despite harm)

Remember patients may suffer from both chronic pain and OUD

May need to “agree to disagree” with the patient

Benefits no longer outweigh risks

“I cannot responsibly continue prescribing opioids as I feel it would cause you more harm than good.”

Always support connection to and/or initiate OUD treatment

35

35

Opioid-Induced Hyperalgesia (OIH)

Paradoxical enhanced pain sensitivity in patients on chronic opioids (> 1 month)

Underlying pathophysiology and true incidence is unknown

No official criteria or guidelines for diagnosing OIH

Clinically pain is generalized, diffuse, ill-defined and not necessarily located at the source of original pain

Increased dose may improve analgesia but only temporarily

Uncertain on whether tapering or switching to a different opioid is more effective

Yi P, Pryzbylowski P. *Pain Med.* 2015
Higgins C, et al. *Br J Anaesth.* 2019

Eisenberg E, et al. *J Pain Symptom Manage.* 2014
Montgomery LS. *J Neurosci Res.* 2022

36

36

Lack or Loss of Benefit

What are the next steps?

- Reassess factors affecting pain
- Re-attempt to treat underlying disease and co-morbidities
- Consider...
 - Add or increase non-opioid and non-pharmacologic treatment
 - Add breakthrough medications
 - Switch to a different opioid (“rotation”)
 - Avoid dose escalation to “high” dose opioids



37

37

Consider Breakthrough Medication

1st Choice:
Non-Opioid

- NSAIDs
- Acetaminophen

IR/SA Opioid

- Same molecule
- Different molecule

Dual Mechanism Opioid

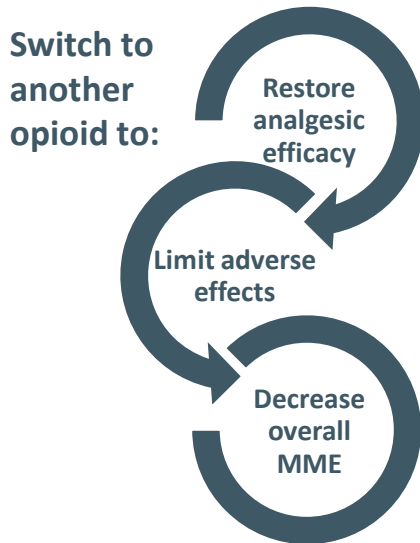
- Tapentadol
- Tramadol

Davies AN, et al. *Eur J Pain*. 2009

38

38

Consider Switching Opioids



- Based on large intra-individual variation in response to different opioids
- Different variants of mu-opioid receptors
- Limited evidence as most trials were retrospective and studied small numbers of patients

Fine PG, Portenoy RK. *J Pain Symptom Manage.* 2009
 Smith HS, Peppin JF. *J Pain Res.* 2014
 Treillet E, et al. *J Pain Res.* 2018

39

39

Opioid Conversion Tables



- Derived from relative potency ratios using single-dose analgesic studies in opioid-naïve patients
- Based on limited doses or range of doses
- Does not reflect clinical realities of chronic opioid administration
- Are not reliable due to individual pharmacogenetic differences
- Most tables do NOT adjust for incomplete cross-tolerance

Opioid	Conversion Factor*
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	5
Methadone	4.7
Morphine	1
Oxycodone	1.5
Oxymorphone	3
Tapentadol+	0.4
Tramadol¥	0.2

www.cdc.gov

Treillet E, et al. *J Pain Res.* 2018
 Webster LR, Fine PG. *Pain Med.* 2012
 Pereira J, et al. *J Pain Symptom Manage.* 2001

40

40

Case Study - Michelle Jones - 54 yo female

Scenario 1a

Switching Opioids



<https://globalrph.com/medcalcs/opioid-pain-management-converter-advanced/>

Rotated off
ER/LA oxycodone
15 mg bid
(45 MME)

Converted to
ER/LA morphine
15 mg bid
(30 MME)

ADVANCED OPIOID CONVERTER	
Converting From:	
First selection: Oxycodone PO	
Daily dose: 30 mg	
Additional drugs to convert if present:	
2nd Selection: 0	
Daily dose: mg	
3rd Selection: 0	
Daily dose: mg	
Reduction for incomplete cross tolerance:	
Reduction factor: 33 %	
— RESULTS —	
Final opiate chosen (Converting TO): Morphine chronic PO	
Equivalent dosage of FINAL opiate: 30.15 mg	

41

41

Case Study - Michelle Jones - 54 yo female

Over the next 18
months after
switching to
morphine



Scenario 1a

- Medication management
 - Continued ER/LA morphine 15mg 2x/day (30 MME)
 - Increased gabapentin to 400mg 3x/day
 - Continued acetaminophen
 - Added nortriptyline 25 mg at night
- Continued acupuncture therapy
- Joined monthly chronic pain support group
- PEG scores remained between 5-6/10
- Remained employed
- Remained adherent with treatment plan and monitoring
- Continued regularly scheduled follow-up visits

42

42

Case Study - Michelle Jones - 54 yo female

Did well on regimen of ER/LA oxycodone 15 mg bid with gabapentin 300 mg 3x/day for 11 months...



Scenario 1a

- Worrisome opioid taking
- Potential loss of benefit
- Switching opioids

Scenario 2

- Patient requested opioid discontinuation

Scenario 3

- Worrisome opioid taking
- Diagnosing and managing opioid use disorder

Scenario 1b

- Continued lack of benefit after opioid switch
- Clinician initiated opioid discontinuation

43

43

Case Study - Michelle Jones - 54 yo female

After switching from oxycodone to morphine...



Scenario 1b

- Pain remained out-of-control (PEG scores 9-10/10)
- After one morphine dose increase, **she requested to be converted back to oxycodone**
- Continued to do poorly: on medical leave from work and spending most of the day in bed (according to her husband)
- On multiple occasions she was confrontational to the office staff when she was unable to be seen by her PCP without an appointment
- She started smoking marijuana to treat her pain

44

44

Cannabis and Pain



Cannabis

- Contains >60 pharmacologically active cannabinoids including cannabidiol (CBD) and the psychoactive tetrahydrocannabinol (THC)
- THC is a schedule I controlled substance (no currently accepted medical use)
- Endocannabinoid receptors are found in high concentration in the brain and spinal cord

Efficacy

- Moderate-quality evidence can be effective for short-term (1-6 m) treatment of neuropathic and nociceptive pain but inconclusive for nociceptive pain
- **For 30% pain reduction** number needed to treat (NNT):
 - 24 for cannabinoids
 - 4-10 for TCAs, opioids, gabapentinoids, SNRIs

Risks/Harms

- Side effects are mild, can cause dizziness, sedation, and impaired coordination
- Long-term use in adolescents and young adults can result in cannabis use disorder and long-term cognitive impairment

Some states have community pharmacists dispense and report medicinal cannabis to the PDMP

Stockings E et al. *Pain* 2018

Noori A et al. *BMJ Open* 2021

Busse JW et al. *BMJ* 2021

McDonagh MS, et al. *Ann Intern Med.* 2022

Ang SP, et al. *Pain Ther.* 2023

45

45

Continued Lack of Benefit

Remember:

- ☐ Not all chronic pain is opioid responsive
- ☐ More opioid is not always better
- ☐ More opioid may increase risk of adverse effects
- ☐ Some chronic pain improves after opioid taper

Baron MJ, McDonald PW. *J Opioid Manage.* 2006

46

46

Discussing Continued Lack of Benefit

Stress how much you believe the patient's pain severity

Show empathy for the patient's suffering

Express frustration that the medication was not more effective

Focus on patient's strengths and encourage therapies for "coping with" pain

Show commitment to continue managing pain, even without opioids

Schedule close follow-ups during and after taper and change in therapies

47

47

Discontinuing Opioids

- You **do not** have to prove addiction or diversion, only assess and reassess the risk-benefit ratio
- If patient is unable to take opioids safely or is non-adherent with monitoring, then discontinuing opioids is appropriate, even in the setting of benefits
- Need to determine how urgent the discontinuation should be based on the severity of the risks and harms
- Determine if the opioid needs to be tapered due to physical dependence
- Document rationale for discontinuing opioids

**You are NOT
abandoning
the patient,
you are
ABANDONING
THE OPIOID**

Tobin DG et al. *J Gen Intern Med.* 2021

48

48

Opioid Discontinuation Risks

- Observational studies identified harms (suicide and overdose) associated with opioid tapering and discontinuation
- Comparative effectiveness study of ~200,000 individuals on stable* long-term opioid therapy, found opioid tapering was associated with a small absolute increase in opioid overdose or suicide compared with maintaining stable opioid dosages

*no evidence of opioid use disorder or opioid misuse

“Tapering/discontinuation should not be considered a harm reduction strategy for patients receiving stable long-term opioid therapy without evidence of misuse”

James JR, et al. *J Gen Intern Med*. 2019
 Mark TL, Parish W. *J Subst Abuse Treat*. 2019
 Oliva EM, Bowe T, Manhapra A, et al. *BMJ*. 2020
 Hallvik SE, et al. *Pain*. 2022
 Larochelle MR et al. *JAMA open*. 2022

49

49

Risk-Benefit Framework



Useful to avoid pitfalls: “But I really, really need opioids.”
 “Don’t you trust me?”
 “I thought we had a good relationship/I thought you cared about me.”
 “If you don’t give them to me, I will drink/use drugs/hurt myself.”
 “Can you just give me enough to find a new doc?”

Response: “I cannot continue to prescribe a medication that is not helping you (or is hurting you, or both).”

50

50

Case Study - Michelle Jones - 54 yo female



Scenario 1b

- Despite the PCP's best efforts to explain the rationale for opioid taper due to lack of benefit and possible harm (e.g., opioid induced hyperalgesia), she continued to demand higher doses of oxycodone
- She was offered alternative pain treatments including cognitive behavioral therapy
- She became increasingly angry and stood up and stated that she was going to find a new doctor
- She left the office...

51

51

Case Study - Michelle Jones - 54 yo female



Did well on regimen of ER/LA oxycodone 15 mg bid with gabapentin 300 mg 3x/day for 11 months...

Scenario 1a

- Worrisome opioid taking
- Potential loss of benefit
- Switching opioids

Scenario 1b

- Continued lack of benefit after opioid switch
- Clinician initiated opioid discontinuation

Scenario 2

- Patient requested opioid discontinuation

Scenario 3

- Worrisome opioid taking
- Diagnosing and managing opioid use disorder

52

52

Case Study - Michelle Jones - 54 yo female



How will you help
her taper off
oxycodone?



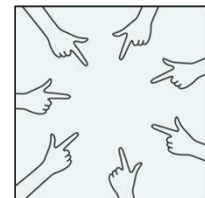
Scenario 2

- Calls the PCP office after she was unable to get her oxycodone refilled due to her insurance's new prior authorization requirement
 - “My insurance keeps refusing to pay for my pain pills which leaves me without them for days.”
- Very upset when describing how badly she is treated by her family, the primary care staff, and at the pharmacy:
 - “I am tired of being treated like a drug addict or criminal.”
 - “I tried to stop but got sick.”
 - “I want to get off these pills!”

53

53

Stigma, Chronic Pain, and Opioids



- Stigma is being discredited, or undesirable, because of an attribute
- Stigma is common among people with chronic pain
- Individuals with pain with less clear pathophysiology report greater stigma
- Stigma can be internalized contributing to poorer pain-related outcomes
 - Positive correlation between stigma and pain intensity, disability, and depression
 - Patients might believe they deserve their pain, are being punished and do not deserve to be included in social activities
- Opioid-related stigma includes fears about anticipated negative attitudes and judgments from others

Hickling LM, et al. *Pain*. 2024
Bulls HW, et al. *Pain*. 2022

54

54

Tapering Opioids



- No validated protocols in patients on opioids for chronic pain
- Very low-quality evidence suggests several types of opioid tapers may be effective and that pain, function, and quality of life may improve for some patients with decrease opioid dose
- Study found 62% of patients in a pain clinic completed a voluntary, patient-centered opioid taper over 4 months with >50% dose reduction
 - Neither pain intensity nor pain interference increased with opioid reduction
 - Success was not predicted by starting dose, baseline pain intensity, years prescribed opioids or any psychosocial variable
- Study of over 100,000 patients on long-term opioids found annual tapering has increased and more likely in women and those on higher opioid doses

Frank JW, et al. *Ann Intern Med.* 2017
 Darnall BD, et al. *JAMA Intern Med.* 2018
 Fenton JJ et al. *JAMA Network Open.* 2019

55

55

Opioid Tapering: General Approach

Speed and Goal
 (decrease dose or discontinuation)
 depends on reason for taper

- Lack of benefit taper over weeks to months
- Apparent harm/risk taper over days to weeks
- Build up alternative pain treatments as short-term withdrawal can lead to transitory increased pain flares

**A Patient Centered
 Approach
 to Opioid Tapering at:**
www.SCOPEofpain.org
 click on: Supplemental Training

1st STEP
 Reduce medication dose
 to the smallest dosage unit

CDC Recommendation

- Decrease 10%/month if on opioids for years
- Decrease 10%/week if on opioids for weeks to months

Dowell D, et al. *MMWR.* 2022

2nd STEP
 Increase amount of time
 between doses

- IR opioid can be started when at lowest ER/LA opioid dose
- Can use α 2-adrenergic agonist (e.g., lofexidine, clonidine*, tizanidine*) to treat withdrawal symptoms

*Off-label

56

56

Case Study - Michelle Jones - 54 yo female



Scenario 2

- Over 6 months she successfully tapered off oxycodone
- Her neuropathic pain was moderately well controlled on combination of nortriptyline 25 mg at night, gabapentin 600 mg 3 times per day and capsaicin cream 3-4 times per day
- Joined a monthly chronic pain support group
- PEG scores remained between 4-5/10 (patient stated she was surprised her pain improved off oxycodone)
- Remained employed
- Remained adherent with the treatment plan and monitoring
- Continued with regularly scheduled follow up visits

57

57

Case Study - Michelle Jones - 54 yo female



Did well on regimen of ER/LA oxycodone 15 mg bid with gabapentin 300 mg 3x/day for 11 months...

Scenario 1a

- Worrisome opioid taking
- Potential loss of benefit
- Switching opioids

Scenario 1b

- Continued lack of benefit after opioid switch
- Clinician initiated opioid discontinuation

Scenario 2

- Patient requested opioid discontinuation

Scenario 3

- Worrisome opioid taking
- Diagnosing and managing opioid use disorder

58

58

Case Study - Michelle Jones - 54 yo female



Scenario 3

- UDTs were consistently positive for oxycodone as expected except once her UDT was opiate positive (i.e., morphine and/or codeine) and oxycodone negative raising the concern for opioid misuse including diversion
 - She denied sharing or giving her oxycodone to others
 - Urine “quantity not sufficient” for confirmation testing
- Unexpected UDT resulted in increased monitoring frequency with no additional unexpected UDTs over the ensuing two months

59

59

Discussing Possible Diversion



- Prescription drug diversion is one form of opioid misuse and is defined as the giving, selling, or trading prescription medications
 - Surveys* indicate that relatives and friends are a common source of diverted opioids
- Discuss why you are concerned about diversion
 - e.g., UDT negative for prescribed opioid, nonadherence with pill counts
- Discuss your inability to continue to prescribe opioids if the opioids are being diverted to others

SAMHSA. (2023). 2022 NSDUH

60

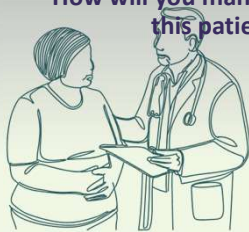
60

Case Study - Michelle Jones - 54 yo female



2 months later...
brought to ED by
ambulance after
suffering an opioid
overdose

How will you manage
this patient?



Scenario 3

- Husband found her unresponsive, administered intranasal naloxone with brisk response and called 911
- In the ED, husband reported that his wife has been running out of her oxycodone, and taking her father's morphine
- Husband had been in denial of how bad his wife's problem had gotten. He reported that she's been fired from her job for missing too many deadlines, and that she once fell asleep with a stove burner on, and melted a teapot
- He heard a staff person in the ED refer to his wife as a "drug abuser"

61

61

Words Matter

 Stigmatizing Language	Non-Stigmatizing Language 
Addict, substance abuser, alcoholic	Person with a substance use disorder (SUD)
Substance abuse	Substance use
Clean urine	Expected test result
Patient is clean	Person with SUD in remission
Dirty urine	Unexpected test result
Patient is dirty	Active substance use

Botticelli MP, Koh HK. *JAMA*. 2016. Kelly JF, Wakeman SE, Saitz R. *Am J Med*. 2015

"Stigma surrounding SUD is perpetuated by the stigmatizing terminology used in healthcare settings, by the news and other media, and by society as a whole."

Zwick J, Appleseth H, Arndt S. *Subst Abuse Treat Prev Policy*. 2020

62

62

Treatment Gaps Following Opioid Overdose

Opioids were dispensed to 91% of patients after a nonfatal overdose

n=2,848

- **7%** had repeat opioid overdose
- At 2 years, cumulative incidence of repeated overdose was **17%** for patients on **high opioid dosages** after the index overdose

Less than a third of opioid overdose survivors receive medications for OUD (MOUD) in the subsequent 12 months

n= 17,568

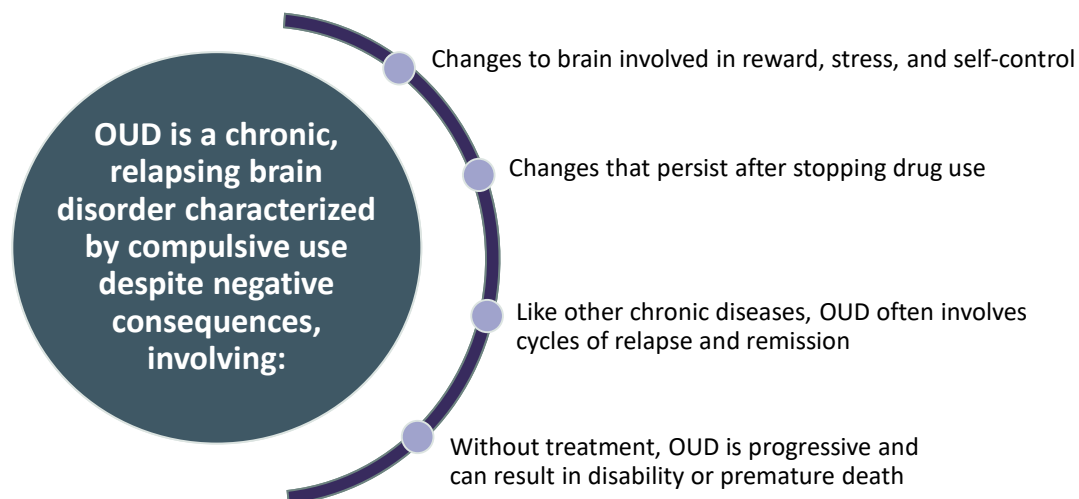
- Receipt of MOUD was associated with decreased all-cause and opioid-related mortality

Larochelle MR, et al. *Ann Intern Med.* 2016
Larochelle MR, et al. *Ann Intern Med.* 2018

63

63

Opioid Use Disorder (OUD)

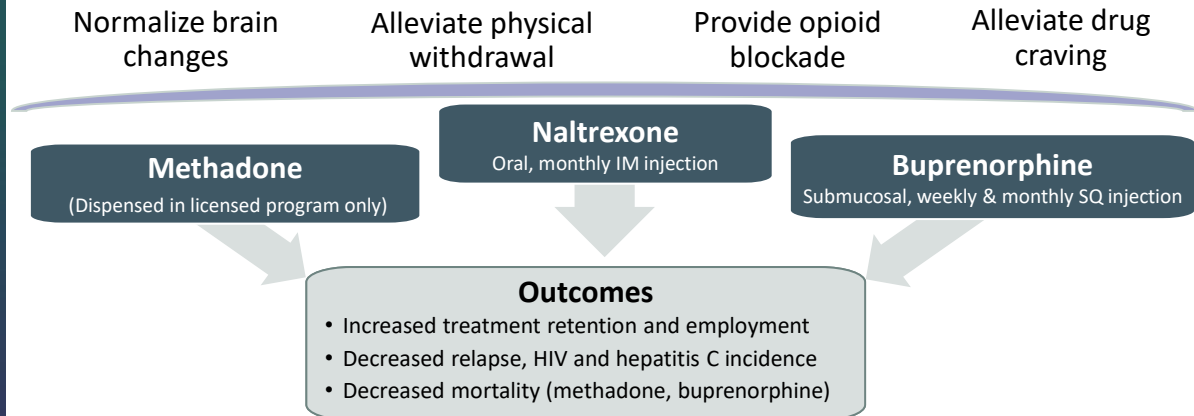


Volkow ND, Koob GF, McLellan AT. *N Eng J of Med.* 2016
Sordo L, et al. *BMJ.* 2017

64

64

Medications for OUD (MOUD)



- Offer or arrange evidence-based medications for treating OUD
- Detox only is not recommended due increased risks for relapse, overdose and death

Recommendation 12

Dowell D, et al. MMWR. 2022

65

65

Case Study - Michelle Jones - 54 yo female



Over the next
6 months...

How will you manage
this patient
perioperatively?



Scenario 3

- PCP continues buprenorphine for the treatment of OUD but doses it 3 times per day to treat both her pain and OUD
- Right hip pain from end-stage arthritis is affecting her quality of life despite trying nonoperative management
- She is schedule for a right hip arthroplasty

66

66

Acute Pain in Patients on MOUD

Systematic Review

There is a growing consensus on perioperative management of patients on MOUD

Patients with OUD history are often more sensitive to painful stimuli

Continue methadone or buprenorphine throughout the perioperative period

Treat pain with analgesics on top of the patient's daily MOUD

Patients taking MOUD may need higher doses of opioid analgesics

Ineffective pain management can result in disengagement in care

Buonora MJ, et al. *Ann Intern Med.* 2025
Veazie S et al. *J Gen Intern Med.* 2020
Kohan L, et al. *Reg Anesth Pain Med.* 2021

67

67

Case Study - Michelle Jones - 54 yo female



Scenario 3

- Did well postop with improved pain control
- Painful diabetic neuropathy well controlled on combination of buprenorphine 4 mg sublingual 3x/day, duloxetine 30 mg 2x/day and nortriptyline 25 mg at night (Note: gabapentin discontinued due to misuse risk and overdose risk when combined with opioids)
- PEG scores remained between 5-6/10
- OUD in sustained remission with MOUD and counseling
- Remained employed
- Continued with regularly scheduled follow up visits

Hill J, Alford DP. *Semin Neuro.* 2018
Goodman CW, Brett AS. *N Engl J Med.* 2017

68

68

Summary Part 2



- Employ universal precautions but individualize care based on risk
- Continue or modify opioids based on clinical indication and response
- Optimize office systems to involve the entire healthcare team including community pharmacists
- Document benefits, risks, harms and rationale for the plan of care
- Worrisome opioid-taking behavior can signify pain-relief or substance-seeking behaviors or a combination of both
- Decisions to continue, modify or discontinue opioids should be based on risks and benefits and should be well-documented
- Offer MOUD for patients with OUD and continue maintenance methadone or buprenorphine perioperatively

69

69

Post-test and Evaluation



- Complete the post-test with a cumulative score of >70%
- Complete the evaluation
- Download your certificate, worth:
 - 2.5 AMA PRA Category 1 Credits™
 - 2.5 nursing contact hours, or
 - 2.5 ACPE credits

70

70